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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 02/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,728	EATON ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/17/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Not. to com. App. A&B*.

DETAILED ACTION

1. Applicant's preliminary amendment filed on 11 September 2002 is acknowledged and entered. Claims 1-20 are pending and under consideration. The claims are drawn to the nucleotide encoding protein designated PRO1446, also identified as encoded by DNA71277-1636 and ATCC accession number 203285, shown in Figures 113 (nucleic acid) and 114 (protein).

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). **Applicant is required to provide a paper copy of the CRF in response to the Office Action.**

Drawings

4. The Office acknowledges the receipt of the drawings filed 5/8/2002.

Information Disclosure Statement

5. The information disclosure statement, filed 9/17/2002, has been considered. The BLAST results demonstrate that applicants are aware of nucleic acids with identity/homology to the one claimed herein. However, as the BLAST results do not give sufficient identifying information, the Examiner cannot determine if said sequences constitute prior art.

Priority Determination

6. The claimed polypeptide has no utility, see rejection below. Since no utility is disclosed in the priority applications and aren't enabling under 35 U.S.C. 112, as required under 119(e), no priority is granted. Accordingly, priority under 35 U.S.C. 120 is set at the instant filing date, 5/08/02.

Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to the date recited above which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of, and fully enabled for, prior to that date.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 8-10 and 14-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7a.The protein identified as PRO1446 (SEQ ID NO: 114) is not disclosed as being expressed on a cell surface. Accordingly, the limitation that the claimed protein comprises an "extracellular domain" (for example see claims 1, 6 and 14 parts (c) and (d)) is indefinite, as the art does not recognize soluble proteins as having such domains. Further, if the protein had an extracellular domain, the recitation of "the extracellular domain", "lacking its associated signal sequence" (claim 1, 6 and 14, part (d), for example) is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell. Claims 2-5, 8-10 and 15-20 are rejected insofar as they are depended on rejected claims 1, 6 and 14.

7b. Claims that recite that the claimed polynucleotide "hybridizes to" another sequence, such as claim 14, reads on any DNA that is capable of hybridizing. In addition, there is no limiting definition of such in the specification, and the metes and bounds of that which will hybridize are dependent upon the conditions under which the hybridization is performed. As the metes and bounds of what will hybridize to a given sequence are entirely dependent upon the conditions of hybridization and washing, the metes and bounds of the claims cannot be determined. With respect to claim 15, although the further limitation that the hybridization conditions are "stringent" is introduced, the term

"stringent conditions" is also a relative term, and thus is indefinite. Claim 15 is rejected insofar as it is depended on rejected claim 14.

Rejections under 35 U.S.C. §101 and §112

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-20 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well-established utility.

Claims 1-20 are directed to isolated polynucleotides that are 80-100% identical to (a) a sequence encoding polypeptide of SEQ ID NO: 114 or (b) a sequence encoding the polypeptide of SEQ ID NO: 114 lacking signal sequence or (c) a sequence encoding the extracellular domain of SEQ ID NO: 114 or (d) a sequence encoding the extracellular domain of the polypeptide of SEQ ID NO: 114, lacking the signal sequence or (e) a polynucleotide sequence of SEQ ID NO: 113 or (f) a full-length coding sequence of SEQ ID NO: 113 or (g) the full-length coding sequence of the cDNA deposited under ATCC 203285. Dependent claims are directed to polynucleotides that hybridize to the above sequences, vectors and host cells comprising the isolated polynucleotides. The specification discloses the isolation of a polynucleotide sequence, SEQ ID NO: 113, which encodes a protein, SEQ ID NO: 114 which is disclosed as PRO1446 (see page 21). The specification contains numerous asserted utilities the claimed nucleotides, including use as a hybridization probe, in the generation of anti-sense RNA and DNA,

"knock-out" animals, as a diagnostic tool, for therapeutic purposes and for the antibody production. Further, there is no disclosure that the protein encoded by the instant nucleotides is expected to be a transmembrane protein, nor of any extracellular domain. There is no biological activity, expression pattern, phenotype, disease or condition, ligand, binding partner, or any other specific feature that is disclosed as being associated with PRO1446 provided in the specification. In the instant invention, claims are directed to polynucleotide sequences encoding the polypeptide of SEQ ID NO: 114 (PRO1446).

The polynucleotide (cDNA) encoding PRO1446 is disclosed to highly express in normal stomach tissues compared to stomach tumor tissues based on the microarray analysis in Example 18 (see page 143, Table 7). Table 7 also describes that many other DNAs are over expressed in various tumors and normal tissues, based on which the specification made a general assertion that an over expressed protein in a diseased tissue is useful not only as a diagnosis marker for the presence of the disease condition, but also as a therapeutic target for treatment of the disease condition. The asserted utility in diagnosis and treatment is not substantial for the following reasons. The specification does not disclose the biological significance of this high or low expression levels, nor the correlation between the high/low expression of the DNA encoding protein PRO1446 and a predisposition to the onset of stomach tumors, i.e., whether it is the cause or the result of the tumors. Further, there is no supporting evidence to indicate that the polypeptide encoded by the polynucleotide of the instant invention has higher or lower expression in tumor tissues compared to their normal tissue counterparts, and as

such one of skilled in the art would conclude that it is not supported by a substantial asserted utility or a well-established utility.

Although, the specification claims that the polynucleotide is more highly expressed in the normal stomach tumor tissues the specification does not teach what is the normal level of expression, does not indicate how high the expression level is compared to for example, stomach tumors; and does not provide a statistical correlation to the level of expression (for example, there is no indication of how many samples were compared to study the expression). Furthermore, even if the tumor is malignant, the specification fails to describe the type or kind of tumor present in stomach tissues (for example, is it a sarcoma or adenocarcinoma etc.). Without knowing the identity of the tumors, one of skill in art cannot use the polynucleotides for diagnosis or therapeutic purposes as asserted. The specification does not disclose a correlation between any specific disorder and the altered level or form of the claimed polypeptides. In addition, the specification does not teach or describe the function of this yet to be identified polypeptide. With respect to the remaining utilities, none of these asserted utilities is specific for the disclosed PRO1446 encoding polypeptides, as each of the aforementioned utilities could be asserted for any naturally occurring polypeptides, and further, as none of the asserted utilities requires any feature or activity that is specific to the disclosed PRO1446 polypeptides.

The polynucleotide may have utility because either its presence or absence or elevation or reduction is correlated to a disease. If this is not the case, then one must turn to the protein encoded by said polynucleotide to ask, "Does the protein encoded by

the polynucleotide have utility?" This is a critical question because if the protein has utility, then this confers utility upon the polynucleotide from which it is transcribed or translated. However, there is no supporting evidence to indicate that the polypeptide encoded by the nucleotide of the instant invention is more highly expressed in normal tissues compared to the stomach tumor tissues. Therefore, one skilled in the art would conclude that it is not supported by a substantial asserted utility or a well-established utility.

Cancerous tissue is known to be aneuploid, that is, having an abnormal number of chromosomes (see Sen, 2000, Curr. Opin. Oncol. 12: 82-88). The data presented in the instant specification are not corrected for aneuploidy. A higher amplification of a gene does not necessarily mean higher expression or lower in a tissue, but can merely be an indication that the cancer tissue is aneuploid. The preliminary data of the instant invention was not supported by further analysis of mRNA or protein expression, for example. Also, the literature reports that it does not necessarily follow that an increase in gene copy number results in increased gene expression and increased polypeptide expression, such that the claimed polypeptides would be useful for diagnosis of cancer or as a drug target. In addition, there is no correlation between WISP-2 mRNA expression and colon tumors. This fact is documented by Pennica et al. (1998, PNAS USA 95:14717-14722). In addition, they also observed that there was no correlation between WISP-2 mRNA expression and colon tumors. Furthermore they disclose that:

> "An analysis of *WISP*-1 gene amplification and expression in human colon tumors showed a correlation between DNA

> amplification and overexpression, whereas overexpression of *WISP*-3 RNA was seen in the absence of DNA amplification. In contrast, *WISP*-2 DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient."

See p. 14722, second paragraph of left column; pp. 14720-14721, "Amplification and Aberrant Expression of *WISPs* in Human Colon Tumors." For example, WISP-2 RNA expression was significantly lower in the tumor than the mucosa (see p. 14721). Therefore, one cannot extrapolate the expression data provided in the specification to support the implicit assertion that the polynucleotide encoding PRO1446 can be used in cancer diagnosis or therapy.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleotides encoding the polypeptides. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." Brenner v. Manson, 148 USPQ: at 696.

A substantial utility, by definition, is a utility that defines "real world" use, and a utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use is not substantial utility. In the instant case, the

higher expression of the nucleotides encoding PRO1446 in normal stomach compared to stomach tumor tissue (if significant), at the most, is an interesting invitation for further research, experimentation and confirmation as to whether the PRO1446 is useful as a diagnosis marker, or suitable as a therapeutic target for treatment of the tumors. These further research and experimentation, however, is part of the act of invention, and until it has been undertaken, the claimed invention is not considered substantial.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9a. Claims 1-20 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above (Paragraph 6), one skilled in the art clearly would not know how to use the polynucleotide of SEQ ID NO: 113 nor polynucleotides 80, 85, 90, 95 or 99% identical to such, nor which encode a protein 80, 85, 90, 95 or 99% identical to the protein of SEQ ID NO: 114, nor polynucleotides which hybridize to any of the above.

Furthermore, even if a specific and substantial utility were subsequently established they would be enabled only for the polynucleotide of SEQ ID NO: 113 or fragments of such that are usable as hybridization probes and are not enabled for polynucleotides 80, 85, 90, 95 or 99% identical to such, nor which encode a protein 80, 85, 90, 95 or 99% identical to the protein of SEQ ID NO: 114, nor polynucleotides which

hybridize to any of the above because there is n no structural or functional information provided in the specification.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re *Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are directed to isolated polynucleotides having at least 80% identity to a SEQ ID NO: 113 or that encode the protein of SEQ ID NO: 114 with or without its signal peptide, or which encode the extracellular domain of SEQ ID NO: 114 with or without its signal peptide, or polynucleotides at least 80% identical to such encoding polynucleotides. Dependent claims are directed to polynucleotides that hybridize to the above sequences, vectors and host cells comprising the isolated polynucleotides. In the instant application, there is insufficient guidance regarding how to make PRO1446 polynucleotides variants recited in the claims.

The specification also is not enabling for the breadth of claims to polynucleotide molecules that hybridize to the disclosed sequences. It is noted that claims that recite hybridization language fail to provide adequate guidance, and do not recite that the polynucleotide encodes a protein, much less one having a specifically disclosed activity. First of all, it is pointed out that the term "hybridize" or "hybridization" generically refers to a process in which a strand of polynucleotide joins or matches up with a

complementary strand through the process of base pairing, wherein the process is basically used to locate or identify DNAs encoding specific proteins. It is well established in the art that 15-20 bases have been considered sufficient to achieve this process. The breadth of the claims includes polynucleotides of as little as 10 nucleotides. With these points in mind, it is the Examiner's position that giving the claims their broadest reasonable interpretation, this language reads on an infinite number of possible DNA sequences for which there is not sufficient enablement without undue experimentation because of the breath of claims, the lack of guidance provided and the quantity of experimentation needed to make or use the invention.

With respect to the hybridization use, as discussed above in paragraph 6 the invention lacks utility and thus lacks enablement. Even if utility were established, the enablement is commensurate in scope only with claims to polynucleotides that are fragments of SEQ ID NO: 113, said fragments of sufficient length to be used as hybridization probes or primers. However, enablement is *not* commensurate in scope with fragments of polynucleotides that differ from SEQ ID NO: 113 due to codon degeneracy, as it is not recognized in the art to use such sequences that are degenerate for such detection or synthesis, and the specification provides no guidance as to how or why to make such degenerate probes or primers. The specification also is not enabling for the breadth of claims to polynucleotide molecules that hybridize to the disclosed sequences because of the quantity of experimentation needed and the lack of guidance provided by the inventor.

The examples provided in the specification do not provide working examples of different DNA sequences that would enable a representative number of the above discussed DNA sequences with assurances that they can be used as probes or primers for the purpose of amplifying or detecting the PRO1446 gene. The mere recitation of this term, and the definitions provided do not serve as sufficient guidance to enable the breadth of the claims for the various DNA sequences claimed. See Ex parte *Forman*, 230 USPQ 546. Since the first paragraph of the statute under 35 U.S.C. 112 requires that there must be an enabling disclosure to support the breadth of the Claims, a review of the specification confirms that the scope of the various DNA sequences that are discussed above have not been enabled. There is but a single polynucleotide disclosed with reference to PRO1446, SEQ ID NO: 113. In the absence of working examples, breadth of claims and sufficient guidance, it would require undue experimentation to enable a commensurate number of the sequences that are encompassed by the claims.

Since the claimed polynucleotides are described at least in part in terms of the protein that might be encoded, the scope of the protein itself must be considered: The specification asserts that PRO1446 is an unspecified secreted and transmembrane polypeptide. However, this family of proteins does not possess a common utility, but rather the proteins that can be broadly classified and have different activities, that confer different uses on them. Accordingly, the mere identification of a protein as belonging to a family, while indicative of evolutionary relatedness, is not indicative of function, nor by extension, of utility. The structure of the putative PRO1446 peptide is briefly discussed

in Figure 122, as having a putative signal sequence, corresponding to amino acids 1-30 and a putative transmembrane domain around amino acids 195-217.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Therefore, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope, i.e. all the polynucleotides with the various percent identities.

9b. Claims 1-5 and 15-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

The claims are drawn to polynucleotides having at least 80%, 85%, 95% or 99% sequence identity with a particular disclosed sequence, or that merely hybridize to a disclosed sequence. The claims do not require that the claimed polynucleotide encode a particular protein, nor that any protein encoded thereby possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. The specification teaches that PRO1446 has (unspecified) homology to secreted and transmembrane polypeptide. The structure of the putative PRO1446 peptide is briefly discussed in Figure 122, as having a putative signal sequence, corresponding to amino acids 1-15. However, there is no functional characteristic associated with these motifs, hence the mere observation that they exist is not probative of function or utility. Further, there is no disclosure that the protein is expected to be a transmembrane protein, nor of any extracellular domain. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1616.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the human sequence.

Therefore, polynucleotides comprising the sequence set forth in SEQ ID NO: 113 or encoding the protein of SEQ ID NO: 114 or fragments thereof sufficiently long to be used as hybridization probes but not the full breadth of the claims meet the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-*

Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless :
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10a. Claims 1-10 and 12-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Lal et al. (WO200000610-A2, 01/2000, Relevant pages are enclosed).

Lal et al. (WO200000610-A2) discloses nucleotides that have 100% overall identity nucleotides encoding the amino acid sequence of SEQ ID NO: 114 of the instant invention (Appendix A). These nucleotides encode a human signal peptide-containing protein (HSPP) that is used to treat or prevent disorders associated with decreased activity or function of HSPP (see page 15, lines 13-15). It is asserted that these proteins may be used in diagnosing, treating or preventing disorders associated with the expression of HSPP. In addition it disclosed nucleotides that are capable of hybridizing to nucleotides encoding polypeptide of SEQ ID NO: 114 of the instant invention. Further, Lal et al. have described the expression of nucleotides containing vectors with promoter sequences in bacterial hosts (page 35, line 5-17). With respect to the limitation of "lacking its associated signal peptide" in claims 8 and 10 as Lal et al. teaches recombinant expression of the said polypeptide, the cDNA would produce the polypeptide identical to the present SEQ ID NO: 114, but lacking its associated signal

peptide when transfected into the host cell, that include for example CHO cells (see page 38, lines 26-33). Thus, meeting the limitations of claims 19-20. Therefore, claims 1-10 and 12-20 are rejected as being anticipated by Lal et al. (WO200000610-A2, 01/2000).

10b. Claims 1-10 and 12-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Jacobs et al. (WO200009552-A1, Pub. 02/2000, relevant pages are enclosed).

Jacobs et al. (WO200009552-A1) discloses nucleotides that have 100% overall identity nucleotides encoding the amino acid sequence of SEQ ID NO: 114 of the instant invention (Appendix B). Jacobs et al. describe human secreted proteins that are encoded by cDNAs that are isolated from various adult and fetal tissues (page 253-332). It is asserted that this proteins for analysis, characterization or therapeutic use. In addition it disclosed nucleotides that are capable of hybridizing to nucleotides encoding polypeptide of SEQ ID NO: 114 of the instant invention. Further, Jacobs et al. have described the expression of nucleotides containing vectors with promoter sequences in bacterial hosts (347, lines 14-30). With respect to the limitation of "lacking its associated signal peptide" in claims 8 and 10 as Lal et al. teaches recombinant expression of the said polypeptide, the cDNA would produce the polypeptide identical to the present SEQ ID NO: 114, but lacking its associated signal peptide when transfected into the host cell, that include for example CHO cells (page 347, lines 24-29). Thus, meeting the limitations of claims 19-20. Therefore, claims 1-10 and 12-20 are rejected as being anticipated by Jacobs et al. (WO200009552-A1, 02/2000).

11. No claims are allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS 01/05

JANET ANDRES
PRIMARY EXAMINER

80	595	100.0	1768	8	ACA95627	Aca95627	Novel hum
81	595	100.0	1768	8	ACD04545	Acd04545	Novel hum
82	595	100.0	1768	8	ACC87986	Acc87986	Human sec
83	595	100.0	1768	8	ACF12648	Acf12648	Human sec
84	595	100.0	1768	8	ACH66300	Ach66300	Novel hum
85	595	100.0	1768	8	ACA96363	Aca96363	Human PRO
86	595	100.0	1768	8	ACA65137	Aca65137	Human PRO
87	595	100.0	1768	8	ACA73863	Aca73863	Human sec
88	595	100.0	1768	8	ACA74275	Aca74275	Novel hum
89	595	100.0	1768	8	ACA96670	Aca96670	Human PRO
90	595	100.0	1768	8	ACD10776	Acd10776	cDNA enco
91	595	100.0	1768	8	ACC91472	Acc91472	Human sec
92	595	100.0	1768	8	ACD02807	Acd02807	cDNA enco
93	595	100.0	1768	8	ACC87372	Acc87372	Human sec
94	595	100.0	1768	8	ACC85956	Acc85956	Human sec
95	595	100.0	1768	8	ACA65444	Aca65444	Human PRO
96	595	100.0	1768	8	ACA94261	Aca94261	Human sec
97	595	100.0	1768	8	ACA98005	Aca98005	Human PRO
98	595	100.0	1768	8	ACA91507	Aca91507	Novel hum
99	595	100.0	1768	8	ACA90721	Aca90721	Novel hum
100	595	100.0	1768	8	ACD16268	Acd16268	Human sec

ALIGNMENTS

```
RESULT 1
AAZ98229
ID   AAZ98229 standard; cDNA; 1545 BP.
XX
AC   AAZ98229;
XX
DT   11-MAY-2000  (first entry)
XX
DE   Human signal peptide containing protein HSPP-121 cDNA SEQ ID NO:255.
XX
KW   Human; signal peptide-containing protein; HSPP; diagnosis; cancer;
KW   inflammation; cardiovascular disease; anticancer; anti-inflammatory;
KW   antimicrobial; nootropic; neuroprotective; cardiovascular; hepatotropic;
KW   antiasthmatic; gene therapy; cell proliferation; neurological disorder;
KW   reproductive disorder; developmental disorder; arteriosclerosis;
KW   cirrhosis; psoriasis; acquired immune deficiency syndrome; anaemia;
KW   asthma; Crohn's disease; infection; Alzheimer's disease; schizophrenia;
KW   Parkinson's disease; Huntington's diseases; ovulatory defect;
KW   muscular dystrophy; ss.
XX
OS   Homo sapiens.
XX
PN   WO200000610-A2.
XX
PD   06-JAN-2000.
XX
PF   25-JUN-1999;   99WO-US014484.
XX
PR   26-JUN-1998;   98US-0090762P.
PR   31-JUL-1998;   98US-0094983P.
PR   01-OCT-1998;   98US-0102686P.
PR   11-DEC-1998;   98US-0112129P.
XX
PA   (INCY-) INCYTE PHARM INC.
XX
PI   Lal P,  Tang YT,  Gorgone GA,  Corley NC,  Guegler KJ,  Baughn MR;
PI   Akerblom IE,  Au-Young J,  Yue H,  Patterson C,  Reddy R,  Hillman JL;
PI   Bandman O;
XX
DR   WPI; 2000-160673/14.
DR   P-PSDB; AAY87344.
XX
PT   New human signal peptide-containing proteins useful in treatment,
PT   prevention and diagnosis of e.g. cancer, inflammation and cardiovascular
PT   disease.
XX
PS   Claim 9; Page 319; 327pp; English.
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CC   AAZ98109 to AAZ98242 encode AAY87224 to AAY87357 which represent the
CC   human signal peptide-containing proteins HSPP-1 to HSPP-134. HSPPs have
CC   anticancer, anti-inflammatory, antimicrobial, nootropic, hepatotropic,
CC   neuroprotective, cardiovascular and antiasthmatic activities, and can be
CC   used in gene therapy. HSPPs can be used to treat or prevent disorders
CC   associated with decreased activity or function of HSPP. Antagonists of
CC   HSPP are used to treat or prevent disorders associated with increased
CC   activity or function of HSPP. Such diseases include cell proliferation
CC   (including cancer), inflammation, cardiovascular, neurological,
CC   reproductive or developmental disorders, (e.g. arteriosclerosis,
CC   cirrhosis, psoriasis, acquired immune deficiency syndrome, anaemia,
CC   asthma, Crohn's disease, microbial or other infections, congestive or
CC   ischaemic heart disease, Alzheimer's, Parkinson's or Huntington's
CC   diseases, schizophrenia, ovulatory defects, muscular dystrophy). HSPP
CC   nucleic acids can be used for the recombinant production of HSPP, for
CC   detecting HSPP in standard hybridisation and amplification assays (for
CC   diagnosis and monitoring), in gene therapy, as antisense, triplex-forming
CC   or ribozyme therapeutics, for detecting related sequences or genetic
CC   variations, and for chromosomal mapping. HSPP are also used to raise
CC   specific antibodies (Ab) and to screen for agonists and antagonists
CC   (potential therapeutic agents). Ab are used to diagnose, or monitor, HSPP
CC   -related diseases (in usual immunoassays), as therapeutic antagonists, in
CC   competitive drug screens, and for purification of HSPP from natural
CC   sources
XX
SQ   Sequence 1545 BP; 347 A; 454 C; 415 G; 329 T; 0 U; 0 Other;

Alignment Scores:
Pred. No.:                2.81e-42        Length:          1545
Score:                    595.00          Matches:         109
Percent Similarity:       100.00%         Conservative:    0
Best Local Similarity:    100.00%         Mismatches:      0
Query Match:              100.00%         Indels:          0
DB:                       3               Gaps:            0

US-10-063-728-114 (1-109) x AAZ98229 (1-1545)

Qy          1 MetLeuTrpTrpLeuValLeuLeuLeuLeuProThrLeuLysSerValPheCysSerLeu 20
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        152 ATGCTGTGGTGGCTAGTGCTCCTACTCCTACCTACATTAAAATCTGTTTTTTGTTCTCTT 211

Qy         21 ValThrSerLeuTyrLeuProAsnThrGluAspLeuSerLeuTrpLeuTrpProLysPro 40
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        212 GTAACTAGCCTTTACCTTCCTAACACAGAGGATCTGTCACTGTGGCTCTGGCCCAAACCT 271

Qy         41 AspLeuHisSerGlyThrArgThrGluValSerThrHisThrValProSerLysProGly 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        272 GACCTTCACTCTGGAACGAGAACAGAGGTTTCTACCCACACCGTCCCCTCGAAGCCGGGG 331

Qy         61 ThrAlaSerProCysTrpProLeuAlaGlyAlaValProSerProThrValSerArgLeu 80
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        332 ACAGCCTCACCTTGCTGGCCTCTCGCTGGAGCAGTGCCCTCACCAACTGTCTCACGTCTG 391

Qy         81 GluAlaLeuThrArgAlaValGlnValAlaGluProLeuGlySerCysGlyPheGlnGly 100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        392 GAGGCACTGACTCGGGCAGTGCAGGTAGCTGAGCCTCTTGGTAGCTGCGGCTTTCAAGGT 451

Qy        101 GlyProCysProGlyArgArgArgAsp 109
              |||||||||||||||||||||||||||
Db        452 GGGCCTTGCCCTGGCCGTAGAAGGGAT 478

RESULT 2
AAA16684
ID   AAA16684 standard; cDNA; 1564 BP.
XX
AC   AAA16684;
XX
DT   16-JUN-2000  (first entry)
XX
DE   Human secreted protein clone qy442_2 nucleotide sequence SEQ ID NO:133.
XX
KW   Human; secreted protein; immunestimulant; immunesuppressant; virucide;
KW   antibacterial; antifungal; cytostatic; antiinflammatory; dermatological;
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KW antidiabetic; antiasthmatic; antiarthritic; antirheumatic; protozoacide;
KW antithyroid; immune deficiency; severe combined immunedeficiency; SCID;
KW infection; HIV; hepatitis; malaria; autoimmune disorder; systemic lupus;
KW connective tissue disease; multiple sclerosis; erythematosis;
KW rheumatoid arthritis; autoimmune pulmonary inflammation; asthma;
KW Guillain-Barre syndrome; autoimmune thyroiditis; myasthenia gravis;
KW insulin dependent diabetes mellitus; graft-versus-host-disease;
KW autoimmune inflammatory eye disease; allergy; ss.
XX
OS Homo sapiens.
XX
PN WO200009552-A1.
XX
PD 24-FEB-2000.
XX
PF 13-AUG-1999; 99WO-US018298.
XX
PR 14-AUG-1998; 98US-0096622P.
PR 17-AUG-1998; 98US-0096815P.
PR 04-SEP-1998; 98US-0099229P.
PR 23-OCT-1998; 98US-0105368P.
PR 08-JAN-1999; 99US-0115234P.
PR 12-FEB-1999; 99US-0119931P.
PR 18-FEB-1999; 99US-0120575P.
PR 30-APR-1999; 99US-0132020P.
PR 11-AUG-1999; 99US-0148424P.
XX
PA (GEMY) GENETICS INST INC.
XX
PI Jacobs K, Mccoy JM, Lavallie ER, Collins-Racie LA, Evans C;
PI Merberg D, Treacy M, Agostino MJ, Steininger RJ, Spaulding V;
PI Wong GG, Clark HF, Fechtel K;
XX
DR WPI; 2000-205979/18.
DR P-PSDB; AAY94964.
XX
PT New polynucleotides encoding secreted proteins, which may have e.g.
PT nutritional, chemokine, immune stimulating or suppressing, hematopoiesis
PT regulating, tissue growth, activin/inhibin antiinflammatory or tumor
PT inhibition activity.
XX
PS Claim 142; Page 594; 641pp; English.
XX
CC AAA16618 to AAA16697 encode the human secreted proteins given in AAY94898
CC to AAY94980, isolated from human adult brain, adult thyroid, adult
CC retina, foetal carcinoma, adult blood, adult neural, foetal kidney, adult
CC placenta, adult testis, whole embryo, adult cartilage, kidney, foetal
CC brain, adult thymus, foetal placenta, adult uterus, adult tumour, and
CC adult bladder, cDNA libraries. The polynucleotides and proteins are
CC predicted to have biological activities which would make them suitable
CC for treating, preventing or ameliorating medical conditions in humans and
CC animals. The polynucleotides can be used as markers for tissues in which
CC the protein is preferentially expressed, as molecular weight markers on
CC Southern gels, and as chromosome markers or tags to identify chromosomes
CC or to map gene positions. The proteins can be used in the treatment of
CC immune deficiencies and disorders, such as severe combined
CC immunedeficiency (SCID), as well as viral, bacterial, fungal and other
CC infections. These infections include human immunodeficiency virus (HIV),
CC hepatitis, herpesviruses, mycobacteria, Leismania spp., malaria and
CC candidiasis. The proteins can be used to treat autoimmune disorders such
CC as connective tissue disease, multiple sclerosis, systemic lupus
CC erythematosis, rheumatoid arthritis, autoimmune pulmonary inflammation,
CC Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent
CC diabetes mellitus, myasthenia gravis, graft-versus-host-disease and
CC autoimmune inflammatory eye disease. The proteins can also be used to
CC treat allergic conditions, such asthma. AAA16698 to AAA16774 represent
CC probes for the human secreted proteins from the present invention
XX
SQ Sequence 1564 BP; 386 A; 427 C; 410 G; 341 T; 0 U; 0 Other;

Alignment Scores:

Pred. No.:	2.85e-42	Length:	1564
Score:	595.00	Matches:	109
Percent Similarity:	100.00%	Conservative:	0
Best Local Similarity:	100.00%	Mismatches:	0
Query Match:	100.00%	Indels:	0
DB:	3	Gaps:	0

US-10-063-728-114 (1-109) x AAA16684 (1-1564)

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Qy          1 MetLeuTrpTrpLeuValLeuLeuLeuLeuProThrLeuLysSerValPheCysSerLeu 20
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        122 ATGCTGTGGTGGCTAGTGCTCCTACTCCTACCTACATTAAAATCTGTTTTTTGTTCTCTT 181

Qy         21 ValThrSerLeuTyrLeuProAsnThrGluAspLeuSerLeuTrpLeuTrpProLysPro 40
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        182 GTAACTAGCCTTTACCTTCCTAACACAGAGGATCTGTCACTGTGGCTCTGGCCCAAACCT 241

Qy         41 AspLeuHisSerGlyThrArgThrGluValSerThrHisThrValProSerLysProGly 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        242 GACCTTCACTCTGGAACGAGAACAGAGGTTTCTACCCACACCGTCCCCTCGAAGCCGGGG 301

Qy         61 ThrAlaSerProCysTrpProLeuAlaGlyAlaValProSerProThrValSerArgLeu 80
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        302 ACAGCCTCACCTTGCTGGCCTCTCGCTGGAGCAGTGCCCTCACCAACTGTCTCACGTCTG 361

Qy         81 GluAlaLeuThrArgAlaValGlnValAlaGluProLeuGlySerCysGlyPheGlnGly 100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        362 GAGGCACTGACTCGGGCAGTGCAGGTAGCTGAGCCTCTTGGTAGCTGCGGCTTTCAAGGT 421

Qy        101 GlyProCysProGlyArgArgArgAsp 109
              |||||||||||||||||||||||||||
Db        422 GGGCCTTGCCCTGGCCGTAGAAGGGAT 448
```

RESULT 3
AAA37106
ID AAA37106 standard; cDNA; 1768 BP.
XX
AC AAA37106;
XX
DT 08-AUG-2000 (first entry)
XX
DE Human PRO1446 (UNQ740) cDNA sequence SEQ ID NO:303.
XX
KW Human; PRO polypeptide; membrane bound protein; receptor; diagnosis;
KW transmembrane; secretion; immunoadhesion; pharmaceutical; screening; ss.
XX
OS Homo sapiens.
XX
PN WO200012708-A2.
XX
PD 09-MAR-2000.
XX
PF 01-SEP-1999; 99WO-US020111.
XX
PR 01-SEP-1998; 98US-0098716P.
PR 01-SEP-1998; 98US-0098749P.
PR 01-SEP-1998; 98US-0098750P.
PR 02-SEP-1998; 98US-0098803P.
PR 02-SEP-1998; 98US-0098821P.
PR 02-SEP-1998; 98US-0098843P.
PR 09-SEP-1998; 98US-0099536P.
PR 09-SEP-1998; 98US-0099596P.
PR 09-SEP-1998; 98US-0099598P.
PR 09-SEP-1998; 98US-0099602P.
PR 09-SEP-1998; 98US-0099642P.
PR 10-SEP-1998; 98US-0099741P.
PR 10-SEP-1998; 98US-0099754P.
PR 10-SEP-1998; 98US-0099763P.
PR 10-SEP-1998; 98US-0099792P.
PR 10-SEP-1998; 98US-0099808P.
PR 10-SEP-1998; 98US-0099812P.
PR 10-SEP-1998; 98US-0099815P.
PR 10-SEP-1998; 98US-0099816P.
PR 15-SEP-1998; 98US-0100385P.
PR 15-SEP-1998; 98US-0100388P.